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FULL PAPER

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Whole-Body Adipose Tissue and Lean Muscle Volumes and Their Distribution across Gender and Age: MR-Derived Normative Values in a Normal-Weight Swiss Population

Erika J. Ulbrich,[1]* Daniel Nanz,[1] Olof Dahlqvist Leinhard,[2] Magda Marcon,[1] and Michael A. Fischer[3]

Purpose: To determine age- and gender-dependent whole-body adipose tissue and muscle volumes in healthy Swiss volunteers in Dixon MRI in comparison with anthropometric and bioelectrical impedance (BIA) measurements.

Methods: Fat–water-separated whole-body 3 Tesla MRI of 80 healthy volunteers (ages 20 to 62 years) with a body mass index (BMI) of 17.5 to 26.2 kg/m^2 (10 men, 10 women per decade). Age and gender-dependent volumes of total adipose tissue (TAT), visceral adipose tissue (VAT), total abdominal subcutaneous adipose tissue (ASAT) and total abdominal adipose tissue (TAAT), and the total lean muscle tissue (TLMT) normalized for body height were determined by semi-automatic segmentation, and correlated with anthropometric and BIA measurements as well as lifestyle parameters.

Results: The TAT, ASAT, VAT, and TLMT indexes (TATi, ASATi, VATi, and TLMTi, respectively) ($L/m^2 \pm$ standard deviation) for women/men were $6.4 \pm 1.8/5.3 \pm 1.7$, $1.6 \pm 0.7/1.2 \pm 0.5$, $0.4 \pm 0.2/0.8 \pm 0.5$, and $5.6 \pm 0.6/7.1 \pm 0.7$, respectively. The TATi correlated strongly with ASATi ($r > 0.93$), VATi, BMI and BIA ($r > 0.70$), and TAATi ($r > 0.96$), and weak with TLMTi for both genders ($r > -0.34$). The VAT was the only parameter showing an age dependency ($r > 0.32$). The BMI and BIA showed strong correlation with all MR-derived adipose tissue volumes. The TAT mass was estimated significantly lower from BIA than from MRI (both genders $P < .001$; mean bias –5 kg).

Conclusions: The reported gender-specific MRI-based adipose tissue and muscle volumes might serve as normative values. The estimation of adipose tissue volumes was significantly lower from anthropometric and BIA measurements than from MRI.

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Key words: total adipose tissue (TAT); lean skeletal muscle tissue (LMT); fat–water-separated MRI; Dixon; age and sex-dependent normative values; whole-body fat

INTRODUCTION

Whole-body tissue-composition analysis with special regard to fat and muscle compartments is a field of intensive research, as changes in fat and muscle volumes and distribution play an important role in the pathogenesis of several diseases (1–7). Although overweight and obesity are related to diabetes mellitus, cancer, depression, cardiovascular diseases and stroke (1–3), muscle volumes are relevant for assessment and diagnosis of muscular dystrophies, inflammatory myopathies (4), spinal cord injuries (5), sports injuries (6), or sarcopenia (7).

In clinical routine, body composition can noninvasively be assessed with several anthropometric methods (8–11). A measure of obesity grade and body fat content is the body mass index (BMI), defined as the ratio of weight and squared height according to the National Institutes of Health/World Health Organization (NIH/WHO) BMI guidelines (8). Other measures, such as skinfold thickness, waist circumference, or waist-to-hip ratio (WHR) estimate abdominal fat mass, whereas body impedance analysis (BIA) provides an estimate of the total amount of adipose and muscle tissue in the body (9,10). However, the accuracy of anthropometric methods and their capability to differentiate subcompartments, such as visceral versus subcutaneous fat, is limited (12,13). Accordingly, imaging methods that directly depict body fat and muscle volumes are being used increasingly. Among these, dual-energy x-ray absorptiometry (DXA) and CT are limited by radiation exposure and a nonspecific classification of fat and muscle tissue based on Hounsfield units (14,15). In comparison, MRI allows for direct accurate quantification of fat and water-bound protons, preferentially based on proton density contrast weighting (16–20) and Dixon-related fat–water-separation methods (21,22).

Recent literature has shown that fat-referenced two-point Dixon imaging provides highly accurate and precise compartmental quantification of adipose tissue and lean tissue volumes (23–27). Moreover, fat-referenced (ie, fat signal normalized to the signal from pure fat voxels)

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lipid quantification effectively eliminates bias in fat concentration estimates as a result of T_1 weighting of the fat and water signal (28). These body composition analyses are of interest, especially in specific populations like patients with metabolic syndrome or myopathy.

A first step in this direction would be represented by a semi-automatic identification of "all fat" and "all water" MR signal voxels and their corresponding volumes.

However, age and gender-dependent normative values of MR-derived adipose tissue and muscle volumes (normalized for body height) are needed that can serve as reference standards for further investigations of pathological changes in diseased patients.

Thus, the purpose of this study is to prospectively evaluate whole-body adipose tissue and muscle volumes in a healthy Swiss population (BMI 17.5 to 26.2 kg/m^2) using fat–water-separated MRI-based acquisition and segmentation methods at 3 Tesla (T), and compare them with anthropometric and BIA measurements.

METHODS

Study Subjects

This prospective, cross-sectional study was approved by the local institutional review board and written informed consent was received from all study subjects. Whole-body MR image data of 104 Swiss volunteers (half women and men) were acquired between 2012 and 2014, all performed with the same MR scanner at our Institute for Diagnostic and Interventional Radiology, from which three other substudies with loosely related partial results (fat-signal fraction (as opposed to fat-volume fraction) measurements in separate organs (liver, gluteal, and lumbar paravertebral muscles), or reporting values from separate image acquisitions (gluteal muscle fat–signal fractions from high-resolution three-point Dixon sequences) were already published (29–31), each with a slightly varying study cohort of 80 subjects. Participants were recruited via local advertisements and via the clinical trials website of our University Hospital. Eighty subjects of generally healthy status with self-reported normal-weight BMI (18.5–25 kg/m^2) and a subsequent actual measured BMI (17.5–26.2 kg/m^2), aged between 20 and 62 years (10 subjects per decade for each gender), were included. Exclusion criteria were general MR contraindications, surgery (especially osteosynthesis), systemic diseases (eg, diabetes, metabolic diseases, chronic obstructive pulmonary diseases, rheumatologic disorders, muscular disorders, chronic pain syndrome, tumors), cardiovascular problems, alcohol addiction, or drug abuse.

Clinical Examination

Height, weight, waist circumference, abdominal girth, hip circumferences, and leg length were measured before the MR examination by one single examiner, and the WHR and BMI (body mass/squared body height) were calculated. Subjects were included only if their BMI proved to be normal (the normal-weight BMI range was extended from 18.5–25 to 17.5–26.2 kg/m^2). Whole-body fat mass percentage was estimated with two bioelectrical impedance instruments via the electrical body resistance through the feet (BIA1; Tanita UM-018, Arlington Heights, IL, USA) or the arms (BIA2; Omron BF300, Kyoto, Japan), with the latter handheld device also estimating the absolute body-fat mass (absBIA2).

All subjects completed a standardized questionnaire (official questionnaire of local Olympics committee named "First Sports Medicine Interview") (32) to assess, for example, the individual's sports activity grade (0 = no sports training, 1 = sports training once a week, 2 = sports training at least twice a week) and lifestyle parameters (weight change and diet within the last 2 years, nicotine and alcohol intake). The volunteers' handedness and leg dominance were noted.

Table 1
Whole-Body Dixon MR Acquisition Parameters of Each Sequence Block

Parameter	Dixon
Number of dimensions	3
Sequence type	3D gradient-echo T_1
Number of echoes	2
Orientation	Tranverse
Acquisition voxel dimensions (mm)	2.0, 2.0, 4.0
Reconstructed voxel dimensions (mm)	1.0, 1.0, 2.0
Interslice gap (mm)	0
Field of view (mm)	560 x 352
Number of sections	80
Repetition time (ms)	4.2
Echo time(s) (ms)	1.2/3.1
Flip angle (°)	5
Number of signal averages	2
SENSE accel. factor (A–P/S–I)	2.0/2.0
Half-scan factor (A–P/S–I)	—
Fold-over direction	AP
Water–fat shift (pixels)	0.292
Receive bandwidth (Hz $pixel^{-1}$)	1485.1
Single-series acquisition time (blocks 1–9) (s)	16.4
Single-series acquisition time (block 10) (s)	32.8
Total acquisition time (10 blocks) (s)	180.4
Max. total acquisition time (including table positioning and prescans) (min)	16

MR Data Acquisition

Whole-body MR data were acquired at 3 T (Ingenia scanner, Philips Healthcare, Best, The Netherlands). The subjects were in supine position with both arms along the body. For signal reception, a 15-element head coil, one of two 16-channel anterior body-array coils, and the 16-channel posterior array coil integrated in the scanner's patient table was used, as required based on the imaged anatomy. For radiofrequency (RF) transmission, the scanner's dual-transmit body coil was used. For each volume, a B_1 map was acquired and used to optimize the RF transmission by applying vendor-specific algorithms, release 4.1.3, the details of which are not transparent to the user.

Axial mDixon images (fat–water-separation two-point mDixon) of the whole body (from head to lower leg) were acquired in 9 to 10 blocks without overlap, depending on the subject's body length, with identical parameters (Table 1), including stacks 3 to 5 from the top with inspiratory breath-holds within the torso. The total

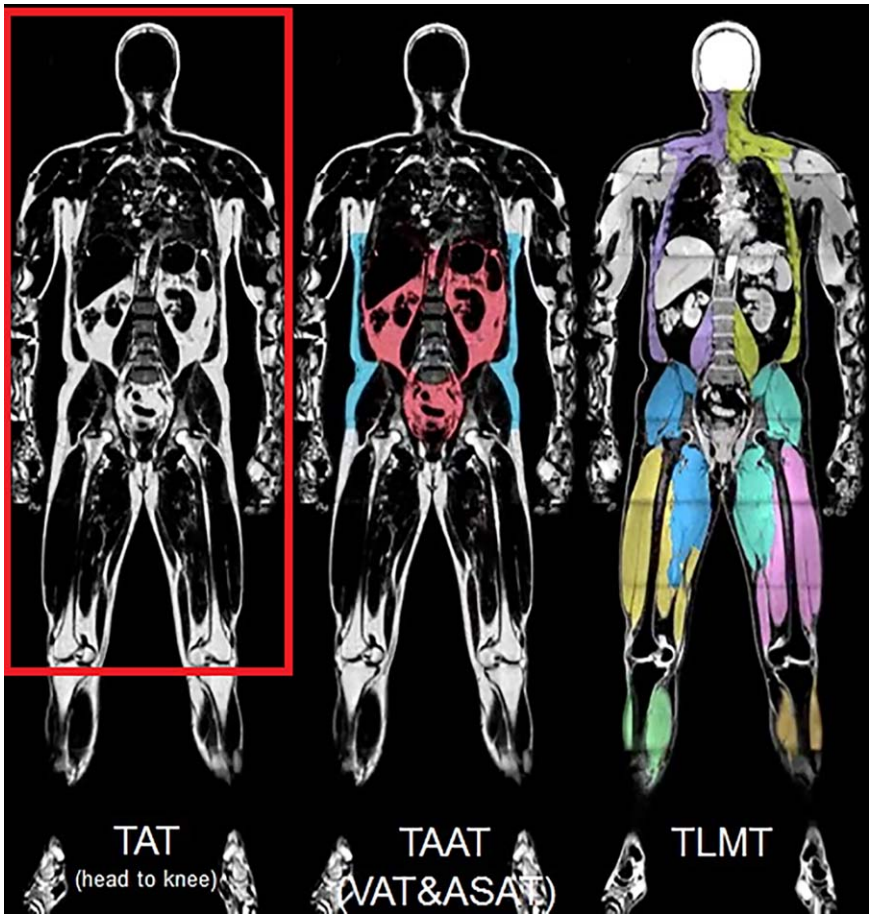

FIG. 1. Segmentation maps with the automatically labeled TAT (**a**), VAT and ASAT (**b**), and the eight muscle groups (**c**) shown in different colors.

nominal duration of the acquisition of the survey and 10 Dixon scans was 3 min, 20 s. This included nine stations with 16-s Dixon scans and a 32-s 10th Dixon scan with a doubled coverage along the superior–inferior direction. However, additional time was required for table repositioning, B_1 and coil-sensitivity calibration scans, and standard prescans. There was a slight interindividual variation in the duration of these scans. The maximum total exam time in cases in which all 10 stations were required for whole-body coverage and excluding the total time for the survey scans (3 min, 40 s) was 16 min.

MR Data Analysis

Automated body composition analysis was performed by the AMRA Profiler online analysis service (Linköping, Sweden), which was blinded to all clinical data and based on previously published methods for fat and muscle segmentation and quantification (24–26,33,34). The analysis was performed on a computation server with a resulting average computational time of 20 min per subject. Before the analysis, major fat and water swaps present in the originally reconstructed water and fat images (primarily separate island swaps related to the top of the liver in the inferior end of the imaging stack) were corrected using an in-house-developed interactive MATLAB (The MathWorks, Natick, MA, USA) tool that allowed the user to identify, segment, and correct misclassified tissue (typical time needed to review each data set was approximately 10 to 15 min per data set). This relates to fat–water swaps introduced by the mDixon phase-sensitive reconstruction algorithm. Further details about the quality control procedure regarding quality and adjustments of automated segmentation results can be found in the recently published work by West et al (35) and Borga et al (24) (the typical time spent to review the segmentation results (to ensure that the data sets were truly well segmented in each compartment throughout the body) in this particular study was approximately 30 min per data set and provided by experienced operators of AMRA).

Each image stack was intensity inhomogeneity–corrected using fat-referenced bias field correction (34). This method uses pure adipose tissue as an internal signal reference. The images were subsequently merged into a composite set of fat and water image volumes covering the whole body. The image volumes were segmented using nonrigid atlas-based registration to assess the following compartments: total abdominal adipose tissue (TAAT) separated into visceral adipose tissue (VAT) and abdominal subcutaneous tissue (ASAT) (24), and total lean muscle tissue (TLMT) separated into left abdomen, right abdomen, left posterior thigh, right posterior thigh, left anterior thigh, right anterior thigh, lower left leg, and lower right leg (26) (Fig. 1c). Furthermore, the total adipose tissue volume (TAT), including all fat signals

within the field of view between the patella and above the head (Fig. 1a), was measured. The VAT (Fig. 1b) was defined as the adipose tissue within the abdominal cavity, excluding adipose tissue outside the abdominal skeletal muscles and adipose tissue and lipids within and posterior of the spine and posterior of the back muscles. The ASAT (Fig. 1b) was defined as subcutaneous adipose tissue in the abdomen from the top of the femoral head to the top of the thoracic vertebrae T9. Adipose tissue and muscle volumes were quantified using a voting scheme based on the registered labels (of up to 31 atlases of both genders with a wide variation of VAT, ASAT, and muscle volumes) and the intensity-corrected fat and water images (26); more detailed information regarding the underlying multi-atlas segmentation technique including a flow diagram of the analysis flow can be found in the papers from Karlsson et al (26) and Borga et al (24). The TAAT was the sum of VAT and ASAT volumes (Fig. 1b), and the TLMT was estimated by summation of all eight muscle groups (Fig. 1c). Measuring the tissue content within each resulting mask, the adipose tissue volume is measured by integrating (summation of the fat signal over all voxels) the fat signal within the mask, whereas the lean tissue volume is measured by subtracting the fat tissue volume from the corresponding tissue mask. This is described in detail in (25,26,33) and (24).

After the automatic atlas-based segmentation, all data sets were visually inspected and quality-assured by an experienced operator (24).

Both arms were excluded from the adipose tissue and muscle volume analysis as a result of insufficient image quality, depending on the size of the volunteers.

All volumes (in liters) were normalized for body height with the following formula: (volume/body height^2)*100, resulting in a volume index (TATi, VATi, ASATi, TAATi, TLMTi). The front and back thigh muscles were grouped into a "thigh" volume and normalized for body weight as thigh/weight.

Statistical Analysis

Descriptive statistics were obtained and their distributions tested for normality with the Kolmogorov-Smirnov test.

Potential volume differences among age subgroups and gender differences of all volumes and volume ratios were tested by analysis of variance with post hoc Bonferroni correction.

Correlation between MRI volume indexes and anthropometric parameters and body fat measures were assessed using Pearson's correlation analysis.

Differences between the mean-value differences in the pairs TAT versus absBIA2 and TAT% versus BIA1 and BIA2, respectively, were tested with the paired sample t-test and by a Bland–Altman evaluation with a 95% confidence interval.

Correlations between MRI volume measurements and age group, lifestyle parameters, sports activity grade, menopause status, and dominant side were assessed with Spearman's rank correlation coefficient.

P values less than .05 were considered significant. When a Bonferroni correction was applied to correct for multiple comparisons regarding age subgroups, a P value less than .0125 was considered statistically significant. All statistical analyses were performed using commercially available software (SPSS, release 22.0, SPSS Inc, Chicago, IL, USA).

RESULTS

The first 80 recruited subjects from the larger study cohort (n = 102) representing all four decades between 20 and 62 years for both genders were included, resulting in a post hoc test power of 80.2% for TATi and 100% power for TLMTi measurements.

Anthropometric and BIA measurements and information regarding lifestyle parameters, sports activity level, dominant side, and menopause status are summarized in Table 2, whereas gender and age-specific MRI-based adipose tissue and muscle volume measurements normalized to body height are shown along with their normalized values (I) in Table 3 and Figure 2. All reported measures were distributed normally.

Age and Gender-Specific Differences of Adipose Tissue and Muscle Compartments

All adipose tissue and muscle volumes showed significant gender differences. The TATi and ASATi were higher in women, and the VATi and TLMTi were higher in men. The VATi differed significantly among the age subgroups in men ($F = 4.482$, $P = 0.009$), whereas there was a tendency toward significant VATi differences among age subgroups in women ($F = 2.660$, $P = 0.063$) (Table 3). The VATi was the only parameter with a significant age dependence for women ($r = 0.426$; $P = 0.006$) and men ($r = 0.324$; $P = 0.041$) (Table 4), with VATi peaking in the fifth decade for men and in the sixth decade for women, respectively (Table 3).

Comparison of Anthropometric, Bioelectrical Impedance, and MRI-Based Measurements

There was a very strong correlation between TATi and ASATi (women/men $r = 0.971/0.936$) and strong correlation between TATi and VATi ($r = 0.759/0.792$). The TAATi and VAT/TAT correlated significantly with several body-fat measures (waist, WHR, BIA) and with VATi, TAATi, and VAT/TAAT for both genders (Table 4; all $r > 0.60$). Women in menopause had significantly higher VAT/TAAT and VAT/TAT (both $P < .01$) than the other women.

Among the anthropometric measures, BMI showed the strongest correlation with TATi ($r = 0.777/0.780$) and ASATi ($r = 0.728/0.724$), whereas VATi correlated best with abdominal circumference in women ($r = 0.698$) and with waist circumference in men ($r = 0.687$). With regard to impedance measurements, MRI-based adipose tissue volumes correlated best with the BIA2 parameters for women ($r = 0.747$) and BIA1 for men ($r = 0.808$). However, estimates of the TAT mass from impedance analysis (absBIA2) were significantly lower than those from MR-

Table 2
Age Group and Gender-Specific Descriptive Statistics of Anthropometric and Bioelectrical Impedance Measurements, Lifestyle Parameters, Handedness and Leg Dominance, and Menopause

	G	20–29	30–39	40–49	50–60	20–60
Age (years)	f	24.6 ± 3.0	33.2 ± 2.9	45.5 ± 3.0	55.1 ± 4.2	39.6 ± 12.2 (21–62)
	m	25.7 ± 3.0	34.6 ± 2.8	42.6 ± 5.4	54.6 ± 4.0	39.4 ± 11.4 (20–61)
Weight (kg)	f	60.6 ± 6.3	59.8 ± 5.5	59.8 ± 7.3	60.7 ± 8.4	60.2 ± 6.7 (43.6–77)
	m	74.7 ± 7.8	73.8 ± 7.7	75.9 ± 8.6	74.8 ± 9.4	74.8 ± 8.1 (56.3–92)
Height (cm)	f	168.5 ± 5.1	168.6 ± 6.7	166.5 ± 6.3	166.8 ± 4.8	167.6 ± 5.6 (158–178)
	m	182.2 ± 8.4	182.7 ± 7.7	180.1 ± 8.5	180.3 ± 6.9	181.3 ± 7.7 (169–200)
BMI (kg/m^2)	f	21.4 ± 2.0	21.1 ± 1.8	21.5 ± 2.3	21.8 ± 2.2	21.4 ± 2.0 (17.5–26)
	m	22.5 ± 1.4	22.1 ± 1.8	23.4 ± 1.5	22.9 ± 1.9	22.7 ± 1.7 (19.4–26.2)
Waist (cm)	f	68.9 ± 4.2	68.4 ± 3.8	72.2 ± 6.7	73.8 ± 6.0	70.8 ± 5.6 (61–85)
	m	81.2 ± 4.2	80.6 ± 4.6	86.4 ± 6.3	84.7 ± 6.3	83.2 ± 5.8 (74–99)
Abdominal girth (cm)	f	76.3 ± 4.5	73.8 ± 5.4	77.4 ± 8.2	81.5 ± 8.6	77.2 ± 7.2 (64.5–94)
	m	86.0 ± 4.5	85.6 ± 7.9	91.2 ± 5.8	89.0 ± 6.1	88.0 ± 6.4 (76–102)
Hip (cm)	f	93.9 ± 7.9	93.3 ± 6.0	92.4 ± 7.8	93.0 ± 6.4	93.2 ± 6.8 (78–109)
	m	99.1 ± 5.2	102.5 ± 21.0	95.8 ± 6.4	97.9 ± 5.8	98.8 ± 11.5 (83–160)
WHR	f	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.9 ± 0.1	0.8 ± 0.1 (0.7–1)
	m	0.9 ± 0.0	0.9 ± 0.1	1.0 ± 0.0	0.9 ± 0.0	0.9 ± 0.1 (0.5–1)
Leg length (cm)	f	81.2 ± 4.7	80.6 ± 7.0	80.8 ± 4.9	80.7 ± 3.5	80.8 ± 5.0 (73–96)
	m	85.9 ± 8.1	87.5 ± 3.5	85.4 ± 6.3	85.4 ± 4.3	86.0 ± 5.6 (71–106)
BIA1 (%)	f	27.1 ± 4.5	26.7 ± 4.1	26.9 ± 5.9	28.1 ± 7.6	27.2 ± 5.5 (12.5–38.7)
	m	14.8 ± 4.2	16.3 ± 3.7	19.6 ± 5.2	18.6 ± 4.0	17.3 ± 4.6 (5.4–31)
BIA2 (%)	f	19.1 ± 3.8	19.0 ± 4.3	22.5 ± 5.6	25.4 ± 5.7	21.5 ± 5.4 (13–33.3)
	m	10.3 ± 3.7	11.7 ± 4.3	16.4 ± 3.8	15.5 ± 4.3	13.5 ± 4.7 (5–22.3)
absBIA2 (kg)	f	11.6 ± 3.2	11.5 ± 3.3	13.7 ± 4.6	16.1 ± 5.8	13.2 ± 4.6 (6.1–26.4)
	m	7.9 ± 3.3	8.8 ± 3.9	12.7 ± 4.1	11.9 ± 4.2	10.3 ± 4.3 (3.4–22.3)
Weight change	f	1	0	0	2	3
(n)	m	1	1	0	0	2
Diet	f	2	1	0	0	3
(n)	m	1	0	0	0	1
Smoker	f	1	0	2	3	6
(n)	m	1	3	3	1	8
Alcohol uptake	f	1	1	4	5	11
(n)	m	6	7	2	2	17
Activity level	f	4/2/4/0	5/1/2/2	5/1/4/0	6/4/0/0	20/4/14/0
(0/1/2/NA)	m	6/0/3/1	3/1/6/0	5/2/2/1	3/0/7/0	17/3/18/0
Handedness	f	8/1/1	9/1/0	9/1/0	9/1/0	35/4/1
(right/left/NA)	m	9/1/0	8/2/0	9/1/0	9/1/0	35/5/0
Leg dominance	f	5/4/1	9/1/0	7/3/0	6/4/0	27/12/1
(right/left/NA)	m	3/7/0	7/3/0	6/4/0	8/2/0	24/16/0
Menopause (n)	f	0	0	2	8	10

G, gender; f, female; m, male; BMI, body mass index; WHR, waist to hip ratio; BIA, body fat percentage measured via stand on (BIA1) and handheld (BIA2) bioelectrical impedance instrument; absBIA2, absolute body-fat volume (kg) via a handheld bioelectrical impedance instrument; weight change and diet, within the last 2 years; n, number of patients; activity levels: 0 = no sports training, 1 = sports training once a week, 2 = sports training at least twice a week; NA, not available.

based measurements (TAT_{mass}) (both genders $P < .001$, mean bias –5 kg) (Fig. 3).

The TLMTi showed only poor negative correlation with TATi and ASATi for both genders (all $r > -0.348$) and with few anthropometric measures (height, abdominal circumference, leg length) in men (all $r > -0.328$). Accordingly, higher thigh/weight correlated moderately to strongly with smaller body fat measures (all $r > -0.317$) for both genders.

Moreover, TATi correlated very strongly with TAATi ($r > 0.96$) and strongly with thigh/weight ($r > -0.79$).

The muscle group volumes did not depend on the volunteers' handedness for both genders. However, in women, the right and left abdominal muscle groups, the left posterior upper leg muscle group, as well as the TLMT correlated with the leg dominance ($r = 0.328$–0.349; all $P < .05$).

Comparison of MRI-Based Adipose Tissue and Muscle Volumes with Lifestyle Parameters and Sports Activity Grade

The TATi ($r = -0.330$, $P = 0.043$) and ASATi ($r = -0.363$, $P = 0.025$) correlated negatively with vegetarian nutrition in men, whereas the TLMTi correlated negatively with alcohol consumption in women ($r = -0.429$, $P = 0.007$). Beyond these, no significant correlations between adipose tissue and muscle volumes versus lifestyle parameters (weight change, diet, nicotine) and sports activity grade were found.

DISCUSSION

In this cross-sectional study we report on age and gender-dependent reference standards for whole-body

Table 3
Age and Gender Depended Descriptive Statistics of Adipose Tissue and Muscle Volume Measurements Normalized to Body Height Derived from Water–Fat-Separated MRI

	G	20–29	30–39	40–49	50–60	20–60	*F*	*P*
TAT	f	18.5 ± 4.0	17.8 ± 3.5	17.2 ± 5.0	18.7 ± 7.1	18.0 ± 4.9; 16.5, 19.6	0.176	0.912
	m	15.5 ± 4.0	16.9 ± 6.0	20.4 ± 6.5	16.9 ± 6.8	17.4 ± 6.0; 15.5, 19.3	1.252	0.305
TAT_{mass}	f	17.4 ± 3.8	16.7 ± 3.3	16.2 ± 4.7	17.6 ± 6.7	17.0 ± 4.6; 15.5, 18.4	0.176	0.912
	m	14.6 ± 3.8	15.9 ± 5.6	19.2 ± 6.1	15.9 ± 6.4	16.4 ± 5.6; 14.6, 18.2	1.252	0.305
TAT_{mass}%	f	28.6 ± 4.7	28.0 ± 4.9	26.8 ± 6.0	28.3 ± 7.9	27.9 ± 5.8; 26.1, 29.8	0.163	0.921
	m	19.3 ± 3.6	21.1 ± 5.7	25.1 ± 6.6	20.7 ± 6.2	21.6 ± 5.9; 19.7, 23.4	1.929	0.142
TATi	f	6.5 ± 1.4	6.3 ± 1.4	6.2 ± 1.9	6.7 ± 2.4	6.4 ± 1.8; 5.9, 7.0	0.113	0.952
	m	4.6 ± 1.1	5.0 ± 1.7	6.3 ± 1.9	5.2 ± 1.9	5.3 ± 1.7; 4.7, 5.8	1.832	0.159
VAT	f	1.0 ± 0.1	1.1 ± 0.3	1.2 ± 0.5	1.5 ± 1.0	1.2 ± 0.6; 1.0, 1.4	2.671	*0.062*
	m	1.6 ± 0.5	2.4 ± 1.2	3.7 ± 1.7	2.7 ± 1.6	2.6 ± 1.5; 2.1, 3.1	4.065	**0.014**
VATi	f	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.2	0.6 ± 0.3	0.4 ± 0.2; 0.4, 0.5	2.66	*0.063*
	m	0.5 ± 0.2	0.7 ± 0.4	1.1 ± 0.6	0.8 ± 0.4	0.8 ± 0.5; 0.7, 0.9	4.482	**0.009**
ASAT	f	4.9 ± 1.9	4.3 ± 1.3	4.3 ± 1.7	4.4 ± 3.0	4.6 ± 2.0; 4.0, 5.2	0.295	0.829
	m	3.7 ± 1.3	3.9 ± 2.1	4.6 ± 1.5	3.5 ± 1.8	3.9 ± 1.7; 3.4, 4.5	0.833	0.484
ASATi	f	1.7 ± 0.7	1.5 ± 0.6	1.6 ± 0.7	1.7 ± 1.0	1.6 ± 0.7; 1.4, 1.9	0.22	0.882
	m	1.1 ± 0.4	1.2 ± 0.6	1.4 ± 0.5	1.1 ± 0.5	1.2 ± 0.5; 1.0, 1.4	1.098	0.363
TAAT	f	5.9 ± 2.0	5.4 ± 1.4	5.5 ± 2.2	6.6 ± 3.8	5.8 ± 2.5; 5.0, 6.6	0.472	0.704
	m	5.3 ± 1.5	6.3 ± 2.8	8.3 ± 3.0	6.3 ± 3.3	6.5 ± 2.8; 5.6, 7.5	2.116	0.115
TAATi	f	2.1 ± 0.7	1.9 ± 0.6	2.0 ± 0.9	2.3 ± 1.3	2.1 ± 0.9; 1.8, 2.4	0.401	0.753
	m	1.6 ± 0.4	1.9 ± 0.8	2.6 ± 1.0	1.9 ± 0.9	2.0 ± 0.9; 1.7, 2.3	2.648	*0.064*
VAT/TAAT	f	0.184 ± 0.05	0.210 ± 0.07	0.215 ± 0.04	0.258 ± 0.05	0.217 ± 0.06; 0.198, 0.236	3.232	**0.034**
	m	0.311 ± 0.08	0.392 ± 0.11	0.429 ± 0.07	0.436 ± 0.07	0.392 ± 0.10; 0.361, 0.422	4.489	**0.009**
VAT/TAT	f	0.055 ± 0.01	0.062 ± 0.02	0.067 ± 0.02	0.083 ± 0.02	0.067 ± 0.02; 0.061, 0.073	4.513	**0.009**
	m	0.110 ± 0.03	0.145 ± 0.06	0.173 ± 0.05	0.156 ± 0.04	0.145 ± 0.05; 0.129, 0.161	3.924	**0.016**
TLMT	f	15.4 ± 1.7	16.4 ± 2.8	15.4 ± 2.3	15.8 ± 2.4	15.7 ± 2.2; 15.0, 16.4	0.417	0.742
	m	24.3 ± 2.0	23.3 ± 1.9	22.3 ± 3.0	23.0 ± 2.1	23.2 ± 2.3; 22.5, 24.0	1.331	0.279
TLMTi	f	5.4 ± 0.5	5.7 ± 0.7	5.6 ± 0.7	5.6 ± 0.7	5.6 ± 0.6; 5.4, 5.8	0.43	0.733
	m	7.3 ± 0.6	7.0 ± 0.9	6.9 ± 0.4	7.1 ± 0.7	7.1 ± 0.7; 6.9, 7.3	0.912	0.445
R	f	2.5 ± 0.4	2.7 ± 0.4	2.6 ± 0.4	2.5 ± 0.5	2.5 ± 0.4; 2.4, 2.7	0.536	0.661
Abd	m	4.1 ± 0.4	3.9 ± 0.5	3.8 ± 0.6	3.9 ± 0.4	3.9 ± 0.5; 3.8, 4.1	0.903	0.449
L	f	2.5 ± 0.4	2.6 ± 0.5	2.5 ± 0.4	2.5 ± 0.5	2.5 ± 0.4; 2.4, 2.6	0.486	0.694
Abd	m	4.1 ± 0.3	3.9 ± 0.4	3.7 ± 0.5	3.8 ± 0.3	3.9 ± 0.4; 3.7, 4.0	1.81	0.163
R Thigh	f	1.5 ± 0.1	1.6 ± 0.3	1.4 ± 0.2	1.4 ± 0.3	1.5 ± 0.2; 1.4, 1.5	0.866	0.467
Front	m	2.5 ± 0.3	2.3 ± 0.2	2.2 ± 0.3	2.2 ± 0.2	2.3 ± 0.3; 2.2, 2.4	2.217	0.103
L Thigh	f	1.4 ± 0.1	1.5 ± 0.3	1.4 ± 0.2	1.3 ± 0.3	1.4 ± 0.2; 1.3, 1.5	0.839	0.482
Front	m	2.3 ± 0.3	2.3 ± 0.3	2.1 ± 0.2	2.2 ± 0.2	2.2 ± 0.3; 2.1, 2.3	1.877	0.151
R Thigh	f	2.6 ± 0.3	2.8 ± 0.5	2.6 ± 0.4	2.7 ± 0.4	2.7 ± 0.4; 2.5, 2.8	0.47	0.705
Back	m	4.1 ± 0.3	3.9 ± 0.4	3.6 ± 0.6	3.9 ± 0.5	3.9 ± 0.5; 3.7, 4.0	1.48	0.236
L Thigh	f	2.5 ± 0.3	2.7 ± 0.6	2.6 ± 0.4	2.8 ± 0.4	2.6 ± 0.4; 2.5, 2.8	0.892	0.455
Back	m	4.0 ± 0.4	3.8 ± 0.4	3.6 ± 0.5	3.8 ± 0.4	3.8 ± 0.4; 3.6, 3.9	1.552	0.218
R Lower	f	1.2 ± 0.1	1.3 ± 0.1	1.2 ± 0.3	1.3 ± 0.2	1.3 ± 0.2; 1.2, 1.3	0.559	0.646
Leg	m	1.7 ± 0.2	1.7 ± 0.2	1.7 ± 0.3	1.7 ± 0.3	1.7 ± 0.2; 1.6, 1.7	0.057	0.982
L Lower	f	1.2 ± 0.1	1.3 ± 0.1	1.2 ± 0.3	1.3 ± 0.2	1.2 ± 0.2; 1.2, 1.3	0.742	0.534
Leg	m	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.3	1.6 ± 0.2	1.6 ± 0.2; 1.5, 1.7	0.318	0.812
Thigh/Weight	f	0.131 ± 0.01	0.143 ± 0.02	0.135 ± 0.02	0.138 ± 0.02	0.136 ± 0.02; 0.130, 0.142	0.683	0.568
	m	0.173 ± 0.02	0.167 ± 0.02	0.151 ± 0.01	0.163 ± 0.02	0.163 ± 0.02; 0.157, 0.170	2.506	*0.074*

Note: Values are reported as mean ± standard deviation (inclusively 95% confidence interval lower, upper bound on the mean) for the different age subgroups for women and men inclusively analysis of variance with post hoc Bonferroni correction (*F* value) of differences among age groups. *P* value < 0.05 was significant, as indicated in bold numbers. *P*-values indicated in italics narrowly achieved significance.
TAT, total adipose tissue (unit: L); TAT_{mass}, total adipose tissue mass, assuming a specific mass for human fat of 0.94 kg/L (unit: kg); TAT_{mass}%, total adipose tissue mass fraction (unit: mass percentage); TAT_i, normalized total adipose tissue (unit: L/m^2); VAT, visceral adipose tissue (unit: L); VAT_i, normalized visceral adipose tissue (unit: L/m^2); ASAT, abdominal subcutaneous adipose tissue (unit: L); $ASAT_i$, normalized abdominal subcutaneous adipose tissue (unit: L/m^2); TAAT, total abdominal adipose tissue = VAT + ASAT (unit: L); $TAAT_i$, normalized total abdominal adipose tissue (unit: L/m^2); TLMT, total lean muscle tissue (unit: L); $TLMT_i$, normalized total lean muscle tissue (unit: L/m^2); R Abd, right abdominal muscles; L Abd, left abdominal muscles; R, right; L, left; Thigh, sum of right and left thigh front and back muscle volume; Thigh/Weight (unit: L/kg).

adipose tissue and lean muscle volumes (before and after normalization to body height) derived from fat–water separating MRI in healthy, Swiss volunteers and on their correlations with common clinically implemented measures of body fat composition and lifestyle parameters. We decided to include only volunteers with normal BMI to measure the normative values of MR-derived adipose tissue and muscle volumes for this population, along with BMI and other anthropometric measures incorporated in the NIH/WHO BMI guidelines (8).

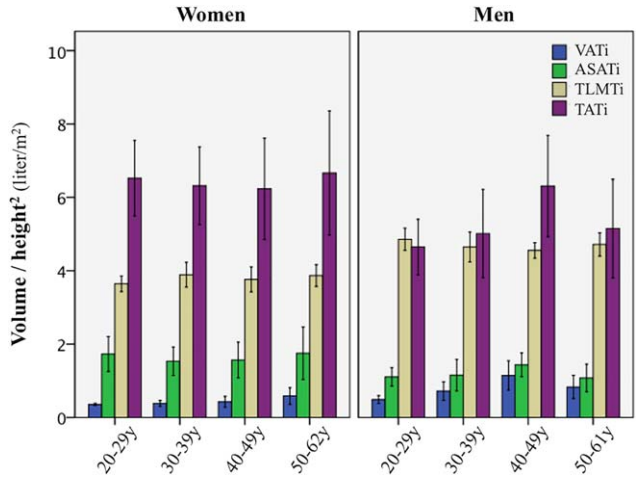

FIG. 2. Age group–averaged adipose tissue and muscle volume indexes (volumes/height^2 (L/m^2)) for both genders subdivided into VATi, ASATi, TATi (from head to knee), and TLMTi (excluding arms) volume indices. All adipose tissue and muscle volume indices showed significant gender differences. The TATi and ASATi were higher in women than in men, and the VATi and TLMTi were higher in men. The VATi also significantly differed among the male age subgroups ($F = 4.482$, $P = 0.009$), peaking in the fourth decade, whereas there was a tendency toward significant VATi differences among the female age subgroups ($F = 2.660$, $P = 0.063$), with VATi peaking in the fifth decade. The VATi was the only parameter with a significant age dependence for women ($r = 0.426$, $P = 0.006$) and men ($r = 0.324$, $P = 0.041$).

It is well known that body tissue composition differs substantially between men and women (36,37). Women generally have a higher percentage of body fat (ie, TAT mass fraction, TAT_{mass}%) than men, which is most likely the result of a lower basal fat oxidation in women (36). Fatty acids are predominately stored in the ASAT in women and in the VAT in men (16). Accordingly, in our study, MRI-based adipose tissue and muscle volumes differed significantly between the two genders, with higher TATi and ASATi in women, but higher VATi, VAT/TAAT, and TLMTi in men. Interestingly, TATi showed a very strong correlation with ASATi and TAATi, but only a moderate to strong correlation with VATi, indicating that imaging of the abdomino-gluteal region (represented as TAAT) might be sufficient for an assessment of total body fat (ie, a shorter MR protocol), and that ASAT and VAT might be partially independent fat depots. Similar to another MRI study in predominantly obese healthy volunteers (16) and consistent with age-related findings regarding liver fat of the same study cohort (31), VATi was the only age-dependent parameter, peaking in the fifth decade for men and in the sixth decade for women (Table 2). Thigh/weight was higher in men for all age groups, which is reasonable because of the higher muscle mass of men. Moreover, thigh/weight was higher in subjects with lower BMI (similar to the negative correlation of TLMTi and TATi), but did not show any significant age dependency in our study cohort.

In a large substudy (38) of the German EPIC cohort, 1192 participants (health status not further specified) between the ages of 35 and 64 with a wide range of BMI (also including the morbidly obese subjects) received a whole-body two-point Dixon MRI with the purpose of comparing TAT, VAT, and SAT with anthropometric data. Reasonably, the fat volumes were higher in this study compared with similar age groups of our study with healthy subjects and normal BMI. Two other studies (20,39) of smaller study populations also reported on larger fat volumes derived from MRI-based quantification in 67 young females and 11 normal-weighted to slightly obese, mostly male patients, respectively. However, the differences may be caused by different morphological criteria of the three study populations, lacking normalization to body height in the other studies, different evaluation methods, and by the exclusion of arms and lower legs in our study and in the study of Neamat-Allah (38).

Among the clinical fat measures, the BMI correlated most strongly with TATi, TAATi, and ASATi in both genders, whereas VATi and TAATi correlated best with abdominal circumference in women and waist circumference in men, which is consistent with previous studies (20,38,40,41). Moreover, in women, WHR correlated positively with a higher VAT portion within the TAAT.

Consistent with a previous study of Machann et al (16), BMI and impedance measures correlated best with MRI-based adipose tissue volumes (TAT, VAT, ASAT) for both genders, but our study showed that anthropometric and BIA measurements significantly underestimated the actual MR-derived adipose tissue volumes.

Our results on whole-body TAT mass fraction, TAT_{mass}%, in women are similar to the DEXA-based NIH/WHO BMI body-fat guidelines (8) (25–35% at 20–39 years; 22–38.5% at 40–60 years, but appeared substantially higher in men: 12–33% versus 8–20% at 20–39 years; 13–35% versus 11–22% at 40–60 years). The higher TAT_{mass}% in men might be the result of the different imaging techniques used for assessment of body constitution, as DEXA assesses body fat based on 2D projection data, even though a recent study already showed high reliability between DEXA and MRI with a small negative bias toward underestimation with MRI (42). Accordingly, DEXA is expected to quantify (eg, VAT, which dominates in the male population) significantly less accurately than an assessment based on a 3D depiction of fat–water compartmentalization, as it is made possible by fat–water-separating MRI.

In our cross-sectional study cohort, women in menopause had significantly higher VAT/TAAT and VAT/TAT than the other women. In a longitudinal study (FELS study) (43) with 472 participants between the ages of 18 and 84, the rate of VAT and SAT accrual, with special emphasis in the menopause transition, was investigated in abdominal MRIs. In this population, both genders continued to accrue abdominal adiposity with age, but the rate of weight and fat gain decreased over time. Moreover, they attribute the gain of VAT in women in menopause rather to an effect of age and not as an effect of the hormonal changes.

Most studies that assessed whole-body muscle volumes examined patients suffering from sarcopenia, which occurs with advancing age (44–46), but also has multiple other contributing factors (7). Interestingly, in

Table 4
Correlation of Anthropometric, Bioelectrical Impedance and MRI-Based Adipose Tissue and Muscle Volume Measurements

	TATi		VATi		ASATi		TLMTi		TAATi		VAT/TAAT		VAT/TAT		Thigh/Weight	
	f	m	f	m	f	m	f	m	f	m	f	m	f	m	f	m
Age group	NS	NS	NS	0.351*	NS	NS	NS	NS	NS	NS	0.473**	0.471**	0.469**	0.452**	NS	NS
Age	NS	NS	0.426**	0.324*	NS	NS	NS	NS	NS	NS	0.464**	0.483**	0.544**	0.423**	NS	NS
Height	NS	NS	NS	NS	NS	NS	NS	−0.375*	NS	NS	NS	NS	NS	NS	NS	NS
Weight	0.563**	0.570**	0.382*	0.348*	0.524**	0.527**	NS	NS	0.518**	0.490**	NS	NS	NS	NS	−0.317*	−0.559**
BMI	0.777**	0.780**	0.560**	0.674**	0.728**	0.724**	NS	NS	0.727**	0.777**	NS	NS	NS	0.385*	−0.534**	−0.580**
Waist	0.578**	0.776**	0.636**	0.687**	0.559**	0.691**	NS	NS	0.607**	0.765**	NS	NS	0.389*	0.372*	−0.348*	−0.665**
Abdominal	0.614**	0.652**	0.698**	0.454**	0.608**	0.636**	NS	−0.328*	0.661**	0.610**	NS	NS	0.431**	NS	−0.346*	−0.628**
Hip	0.627**	NS	0.320*	NS	0.605**	NS	NS	NS	0.569**	NS	−0.364*	NS	NS	NS	−0.440**	NS
WHR	NS	NS	0.488**	0.361*	NS	NS	NS	NS	NS	0.341*	0.358*	NS	0.553**	0.333*	NS	NS
Leg length	NS	NS	NS	NS	NS	NS	NS	−0.372*	NS	NS	NS	NS	NS	NS	NS	−0.325*
BIA2	0.747**	0.705**	0.762**	0.614**	0.713**	0.640**	NS	−0.306	0.762**	0.697**	NS	NS	0.435**	0.320*	−0.517**	−0.643**
absBIA2	0.756**	0.749**	0.746**	0.615**	0.720**	0.666**	NS	NS	0.764**	0.712**	NS	NS	0.385*	NS	−0.493**	−0.649**
BIA1	0.733**	0.808**	0.611**	0.754**	0.720**	0.677**	NS	NS	0.732**	0.792**	NS	NS	NS	0.470**	−0.511**	−0.572**
TATi			0.759**	0.792**	0.971***	0.936***	−0.348**	−0.449**	0.972**	0.962**	−0.321*	NS	NS	0.359*	−0.791**	−0.834**
VATi					0.722***	0.622**	NS	NS	0.827**	0.892**	NS	0.589**	0.778**	0.830**	−0.482**	−0.590**
ASATi							−0.396*	−0.478***	0.986**	0.909**	−0.400*	NS	NS	NS	−0.803**	−0.824**
TLMTi									−0.372*	−0.375*	0.324*	NS	NS	NS	0.701**	0.725**
TAATi											NS	NS	0.332*	0.548**	−0.768**	−0.790**
VAT/TAAT													0.794**	0.877**	0.503**	NS
VAT/TAT											0.794**	0.877**			NS	NS
Thigh/Weight																

Note: Spearman correlation coefficient of volume indexes with age groups and Pearson correlation coefficient (*r* value) of volume indexes with age and body parameters (height; weight; BMI; waist, hip, and abdominal girth measurements; WHR; leg length; BIA1; BIA2; and absBIA2). Also shown are Pearson coefficients that characterize the correlation between the volume indexes (TATi, VATi, ASATi, TLMTi, TAATi) and volume ratios (VAT/TAAT and VAT/TAT).

TAT, total adipose tissue (unit: L); TAT_i, normalized total adipose tissue (unit: L/m^2); VAT, visceral adipose tissue (unit: L); VAT_i, normalized visceral adipose tissue (unit: L/m^2); ASAT, abdominal subcutaneous adipose tissue; $ASAT_i$, normalized abdominal subcutaneous adipose tissue; TAAT, total abdominal adipose tissue = VAT + ASAT (unit: L); $TAAT_i$, normalized total abdominal adipose tissue (unit: L/ m^2); TLMT, total lean muscle tissue (unit: L); $TLMT_i$, normalized total lean muscle tissue (unit: L/m^2); Thigh/Weight (unit: L/g); BMI, body mass index (unit: kg/m^2); NS, not significant.

***Correlation was significant at the 0.001 level (2-tailed). **Correlation was significant at the 0.01 level (2-tailed). *Correlation was significant at the 0.05 level (2-tailed).

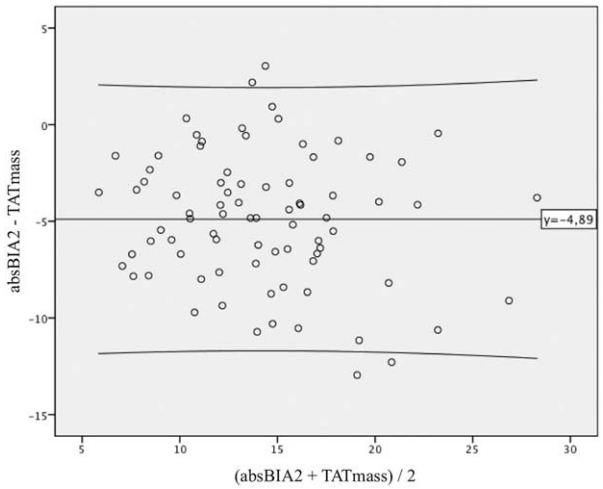

FIG. 3. Bland–Altman plot of difference versus mean of impedance (absBIA2) and MR (TAT) based total fat-tissue mass assessments (TAT_{mass} (unit: kg)). Total body fat estimation by impedance was measured with a handheld device (see M&M). The AbsBIA2 significantly underestimated the total fat mass as determined with the fat–water-separated MRI, showing a mean bias of approximately 5 kg. However, because we excluded arms and lower legs from the MR-based analyses, the mean bias of impedance fat mass quantification might be even greater than determined in our study.

our study group of healthy volunteers between 20 and 60 years, the TLMTi did not change with age. This may be the result of similar activity levels and health awareness across all age groups, as assessed in our questionnaire, and may be a finding congruent with a "modern western lifestyle." Geisler et al reported in a similar study cohort of 346 healthy Caucasian subjects between the ages of 18 and 78 with a BMI of less than 35kg/m^2, consistent results with no significant age dependency of the skeletal muscle mass. Moreover, the DEXA measurements significantly overestimated the MR-derived values by 9.8% (47). In the so-called Rosetta study, healthy controls between the ages of 18 and 40 years undergoing DEXA-based muscle-mass measurements showed skeletal mass–to-height index (SMI) values of 8.6 kg/m^2 (men) and 7.3 kg/m^2 (women) (48). In our study, the measure most closely related to the SMI is the TLMTi (SMI without arm muscles), which showed lower values (7.1 L/m^2 for men; 5.6 L/m^2 for women) than reported in the previously mentioned study. A conversion of our volume-based TLMTi to a corresponding mass-based index would imply multiplication with the average lean-muscle-tissue density, which is unknown but quite certainly larger than 1 g/cm^3 (49). Thus, it would reduce the apparent numerical discrepancies. The remaining differences might, in part, be rationalized by the limitations of the 2D DXA method, with substantial variability depending on the equation used to estimate the lean body mass as well as the different definition of total skeletal muscle volume (50,51). In a recent study (25) using the same segmentation methods (26) as in our study and also excluding arm muscles, similar TLMT volumes (TLMT 19.8 ± 1.9 versus 19.3 ± 9.1 L) were reported. Although no correlation was found between TLMT with BMI in both studies (25), another previously mentioned study (47) measured higher absolute values in MRI (skeletal muscle mass, 25.8 kg) that also included arm muscles, but excluded the head.

No significant left–right difference of muscle-group volumes was found in our study nor correlations with handedness; however, a significant correlation with leg dominance was observed in men.

Although MRI is more time-consuming and expensive compared with DXA, it previously has been attributed with higher accuracy in assessments of body composition. The lack of radiation allows for screening of young and potentially healthy patients as well as for repetitive scanning of severely diseased patients. Accordingly, further MR-based studies evaluating whole-body tissue composition in diseased patients in reference to our study are desirable to determine cut-off values for disease detection and monitoring. Moreover, further studies in healthy subjects are needed to confirm our findings and to propagate normative values for other ethical groups or societies.

CONCLUSIONS

Estimation of adipose tissue volumes was significantly lower from anthropometric and BIA measurements than from MRI. Our study indicates that the region from abdomen to thigh might be sufficient to estimate body fat and muscle mass distribution.

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